

NOTE: This disposition is nonprecedential.

**United States Court of Appeals
for the Federal Circuit**

CEPHALON, INC., ACUSPHERE, INC.,
Plaintiffs-Appellants

v.

ABRAXIS BIOSCIENCE, LLC, CELGENE CORP.,
Defendants-Cross-Appellants

ABRAXIS BIOSCIENCE, INC.,
Defendant

2014-1411, 2014-1442

Appeals from the United States District Court for the
District of Massachusetts in No. 1:11-cv-12226-RGS,
Judge Richard G. Stearns.

Decided: June 17, 2015

GEORGE C. LOMBARDI, Winston & Strawn LLP,
Chicago, IL, argued for plaintiffs-appellants. Also
represented by WILLIAM P. FERRANTI, KARL LEONARD.

GREGORY A. CASTANIAS, Jones Day, Washington, DC,
argued for defendants-cross-appellants. Also represented

by JOHN PATRICK ELSEVIER, ANTHONY M. INSOGNA, PHILIP T. SHENG, San Diego, CA; CHRISTOPHER M. MORRISON, Boston, MA.

Before WALLACH, MAYER, and CHEN, *Circuit Judges*.

WALLACH, *Circuit Judge*.

Plaintiffs-appellants Acusphere, Inc. and Cephalon, Inc. (collectively, “Acusphere”) appeal certain claim construction determinations of the United States District Court for the District of Massachusetts with respect to a patent directed to formulations of, and methods of making, the anticancer drug product paclitaxel. In light of the district court’s construction, Acusphere stipulated to a final judgment of non-infringement. Defendants-cross-appellants Abraxis Bioscience, LLC and Celgene Corp. (collectively, “Celgene”) cross-appeal, asserting certain claim terms of the patent are indefinite. Because the district court properly construed at least some of the disputed terms, this court affirms and does not reach the indefiniteness issues presented by the cross-appeal.

BACKGROUND

Acusphere, Inc. is the assignee of U.S. Reissued Patent No. RE40,493 (“the ’493 patent”), titled “Porous Paclitaxel Matrices and Methods of Manufacture Thereof.” Acusphere, Inc., and its exclusive licensee Cephalon, Inc., sued Celgene for infringement of the ’493 patent based on Celgene’s Abraxane drug product, which contains a fast-dissolving form of paclitaxel.

Paclitaxel is a type of taxane compound derived from the bark of the Pacific yew tree and exhibits “extremely low solubility in water,” ’493 patent col. 1 ll. 22–27, making effective administration challenging. The prior art clinical formulation addressed this problem by the use of a solubilizing agent called Cremophor

(polyoxyethylated castor oil), but this agent can cause severe adverse reactions and requires infusion into the patient over several hours. The '493 patent addresses the solubility problem by integrating paclitaxel into a "porous matrix form which forms nanoparticles and microparticles of paclitaxel when the matrix is contacted with an aqueous medium." *Id.* col. 1 l. 66–col. 2 l. 1.

Following the district court's construction of a number of disputed claim terms, *see Cephalon, Inc. v. Celgene Corp.*, 985 F. Supp. 2d 171 (D. Mass. 2013), Acusphere stipulated to noninfringement. Acusphere appeals the district court's claim constructions of: (1) "nanoparticles" and "microparticles"; (2) "nanoparticles and microparticles of a taxane"; and (3) "wherein upon exposure to an aqueous medium, the matrix dissolves to leave the taxane nanoparticles and microparticles." *See* Appellants' Br. 2–3. Acusphere stipulated that if any of the district court's claim constructions are affirmed, it cannot sustain its burden of proving infringement of the '493 patent. J.A. 29. This court has jurisdiction under 28 U.S.C. § 1295(a)(1) (2012).

DISCUSSION

I. Standard of Review

This court reviews the district court's claim construction *de novo*, but "review[s] for clear error those factual findings that underlie a district court's claim construction." *Teva Pharm. USA, Inc. v. Sandoz, Inc.*, 135 S. Ct. 831, 841–42 (2015).

II. The District Court Correctly Construed "Nanoparticles" and "Microparticles"

All asserted claims require a matrix formed of, among other things, "nanoparticles" and "microparticles" of a taxane. *See, e.g.*, '493 patent col. 12 l. 4. Claim 1 is representative:

A pharmaceutical composition comprising a porous matrix formed of a hydrophilic excipient, a wetting agent and *nanoparticles and microparticles of a taxane*, wherein the *nanoparticles and microparticles* have a mean diameter between about 0.01 and 5 μm and a total surface area greater than about $[0.5 \text{ m}^2] 0.5 \text{ m}^2/\text{mL}$, wherein the porous matrix is in a dry powder form, and wherein upon exposure to an aqueous medium, the matrix dissolves to leave the taxane nanoparticles and microparticles, wherein the dissolution rate of the taxane nanoparticles and microparticles in an aqueous solution is increased relative to unprocessed taxane.

Id. col. 12 ll. 2–12 (first emphasis added; second emphasis indicates an addition made upon reissue; brackets indicate a deletion from the original patent).

The district court construed the term “nanoparticles” to mean “particles that have a mean diameter of between about 1 to 1000 nanometers and less than that of microparticles,” and construed “microparticles” to mean “particles that have a diameter of between about 1 to 1000 microns and greater than that of nanoparticles.” J.A. 28–29; *see also Cephalon*, 985 F. Supp. 2d at 175–78. The district court found these constructions supported by the “widely accepted definition” of the terms nanoparticles and microparticles. *Cephalon*, 985 F. Supp. 2d at 176. It also found “that other Acusphere patents in the same field, many credited to the inventors of the ’493 patent,” define microparticles as ranging from 1 to 1000 microns (μm) and nanoparticles as ranging from 1 to 1000 nanometers (nm). *Id.* The district court also looked to a textbook, entitled *Microparticulate Systems for the Delivery of Proteins and Vaccines*, which further confirmed this understanding.

Acusphere first argues the “widely accepted definition[s]” of the disputed terms are “*not* standard usage.” Appellants’ Br. 18 (quoting *Cephalon*, 985 F. Supp. 2d at 176). As the United States Supreme Court has recently instructed, “how the art underst[ands] [a] term . . . [is] plainly a question of fact.” *Teva*, 135 S. Ct. at 838 (quoting *Harries v. Air King Prods., Co.*, 183 F.2d 158, 164 (2d Cir. 1950) (Hand, C.J.)). Technical words “may give rise to a factual dispute” that, “like all other factual determinations, must be reviewed for clear error.” *Id.* at 837–38. The terms “microparticles” and “nanoparticles” are technical words, and how the relevant scientific community understands them is therefore a question of fact reviewable for clear error.

Acusphere fails to establish clear error. It asserts “there is no *universally* agreed definition of the size of a nanoparticle.” Appellants’ Br. 20 (emphasis modified) (quoting *Cephalon*, 985 F. Supp. 2d at 176). However, the district court described its finding as to how the art understood the terms nanoparticles and microparticles not as “universal” but as “widely accepted.” *Cephalon*, 985 F. Supp. 2d at 176. To the extent Acusphere is arguing the district court committed legal error by basing its construction on an understanding that was less than universally accepted, a definition need not be universally accepted to form a proper basis for claim construction. *See Phillips v. AWH Corp.*, 415 F.3d 1303, 1314 (Fed. Cir. 2005) (en banc) (Claim construction may “involve[] little more than the application of the *widely accepted* meaning of commonly understood words.”) (emphasis added). Furthermore, it was not clear error to credit Acusphere’s other patents in the field or the textbook.¹ Moreover, we

¹ It appears the district court understood the relevant portion of the textbook to be co-authored by one of the named inventors. Although this is incorrect, the

cannot find clear error given that Acusphere's expert, Dr. Robert Langer,² stated "the ordinary meanings of 'nanoparticles' and 'microparticles' are directed to particle size, with 'nanoparticles' referring to particles with a diameter in the nanometer (nm) range and 'microparticles' referring to particles with a diameter in the micrometer (μm) range." J.A. 1550 ¶ 28. In addition, Celgene's expert, Dr. Amiji, described the range of 1 to 1,000 nanometers for nanoparticles, and 1 to 1,000 microns for microparticles as "the accepted definition[s]." J.A. 3100 ll. 5–8, 14–20.

Expert testimony, dictionaries, treatises, and other extrinsic evidence that shed light on the commonly understood meaning of a technical term are "less significant than the intrinsic record in determining the legally operative meaning of claim language." *Phillips*, 415 F.3d at 1317 (internal quotation marks and citations omitted). "[T]he specification may reveal a special definition given to a claim term by the patentee that differs from the meaning it would otherwise possess. In such cases, the inventor's lexicography governs." *Id.* at 1316.

Drawing on this principle, Acusphere asserts the inventors of the '493 patent acted as their own lexicographers of the terms "nanoparticles" and "microparticles" by reciting in the claim itself "nanoparticles and microparticles of a taxane, wherein the nanoparticles and microparticles have a mean diameter between about 0.01 and 5 μm ." Appellants' Br.

district court's recognition of the information in the textbook was nevertheless not clear error.

² Dr. Langer was also a founder of Acusphere and a scientific advisor to it at the time of prosecution of the application that led to the '493 patent. See J.A. 3176 ll. 10–15, 3177 ll. 2–6.

21 (internal quotation marks and citation omitted). However, this claim language requires the mean diameter of the smaller nanoparticles and larger microparticles to be between about 0.01 and 5 μm , and indicates the porous matrix must include particles falling into both size ranges. It does not provide any independent definition of the terms “nanoparticles” or “microparticles.”

By providing only a single range (0.01 to 5 μm), the language could, at most, define the size of *either* nanoparticles *or* microparticles, unless the two terms are construed to have no difference in meaning. Perhaps recognizing this constraint, Acusphere proposes the two terms should be construed as meaning exactly the same thing, namely, “particles of a taxane having a mean diameter between about 0.01 and 5 μm .” Appellants’ Br. 10. However, construing the two terms to have no difference in meaning would render one of the terms superfluous, which is disfavored in claim construction. *See Merck & Co. v. Teva Pharm. USA, Inc.*, 395 F.3d 1364, 1372 (Fed. Cir. 2005) (“A claim construction that gives meaning to all the terms of the claim is preferred over one that does not do so.”); *Power Mosfet Techs., L.L.C. v. Siemens AG*, 378 F.3d 1396, 1410 (Fed. Cir. 2004) (explaining that a claim construction that renders claim terms superfluous is generally disfavored).

In addition, the prosecution history precludes assigning the two terms the same meaning. The predecessor to claim 1 originally recited only “microparticles.” *See* J.A. 1016. A U.S. Patent and Trademark Office examiner rejected the claims as obvious in light of U.S. Patent Nos. 6,096,331 (“Desai”) and 5,855,913 (“Hanes”). In the rejection, the examiner stated that, in view of these references, the use of micron-sized particles would have been known to one having ordinary skill in the art. In response, Acusphere stated “[t]here are no nanoparticles” in Hanes. J.A. 1021. In the same transmittal, it also amended claim 1 by, among other

things, substituting “nanoparticles and microparticles” in place of “microparticles,” without altering the size range of the particles (0.01 to 5 μm). *See* J.A. 1016. Under Acusphere’s construction, a pharmaceutical composition could incorporate only micron-sized particles and still fall within the scope of the claims. Such a construction is inconsistent with Acusphere’s amendment adding “nanoparticles and” to overcome Hanes’s use of only microparticles. Acusphere does not offer an explanation of why the word “nanoparticles” was added during prosecution, stating only “the inventors tweaked their nomenclature” which it claims “was a matter of semantics, not substance.” Appellants’ Br. 33–34. This assertion, however, is unsupported by the prosecution history.

Acusphere argues the district court’s construction of microparticles is inconsistent with dependent claim 6, which claims “[t]he composition of claim 1 wherein the mean diameter of the taxane microparticles is between about 0.50 and 5 μm .” ’493 patent col. 12 ll. 30–31. If “microparticles” must have a minimum diameter of 1 μm , Acusphere reasons, it would be impossible for the mean diameter of a composition of such particles to be 0.50 μm , as claim 6 requires. This inconsistency could perhaps be explained by the addition elsewhere of the term “nanoparticles” during prosecution, in combination with an inadvertent failure to consistently amend the claims. *See Cephalon*, 985 F. Supp. 2d at 177 n.2 (“Any inconsistency, however, is a product of Acusphere’s at times seemingly random omission of the term ‘nanoparticles’ in the patent.”).

In any event, the lexicography exception requires the patent drafter to “clearly set forth a definition of the disputed claim term.” *Aventis Pharma S.A. v. Hospira, Inc.*, 675 F.3d 1324, 1330 (Fed. Cir. 2012) (quoting *Thorner v. Sony Computer Entm’t Am. L.L.C.*, 669 F.3d 1362, 1365 (Fed. Cir. 2012)). If, as Acusphere asserts, the

range of 0.01 to 5 μm specified in claim 1 constitutes a definition of “microparticles,” it is unclear why nearly identical language in claim 6 would not also constitute a definition. However, claim 6 provides a *different* range of 0.50 to 5 μm , which would yield two different definitions of “microparticles.” These inconsistent “definitions” do not “clearly set forth a *definition* of the disputed claim term” as required by this court’s precedent. *Id.* (emphasis added) (internal quotation marks and citation omitted). The district court therefore correctly construed the terms “microparticles” as “particles that have a diameter of between about 1 to 1000 micrometers and greater than that of nanoparticles” and “nanoparticles” as “particles that have a diameter of between about 1 to 1000 nanometers and less than that of microparticles.” J.A. 28–29.

Acusphere stipulated that under the district court’s constructions of any one of the terms “nanoparticles,” “microparticles,” “nanoparticles and microparticles of a taxane,” or “wherein upon exposure to an aqueous medium, the matrix dissolves to leave the taxane nanoparticles and microparticles,” Acusphere cannot sustain its burden of proving infringement of the ’493 patent. J.A. 29. Because this court affirms the district court’s construction of “nanoparticles” and “microparticles,” this court does not reach the construction of the remaining terms. *See Uship Intellectual Props., LLC v. United States*, 714 F.3d 1311, 1313 n.1 (Fed. Cir. 2013) (“Because construction of ‘validating’ resolves this case, we need not reach the parties’ arguments with regard to ‘storing.’”).

CONCLUSION

For these reasons, the decision of the district court is

AFFIRMED